

Assessing the corneal sub-basal nerve plexus by *in vivo* confocal microscopy in patients with blepharoptosis

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ABSTRACT

Background: To assess *in vivo* confocal microscopy features of corneal sub-basal nerve plexus in patients with congenital or aponeurogenic blepharoptosis using a fully automated software (ACCMetrics).

Patients and methods: This prospective study included 33 patients with blepharoptosis and 17 normal controls. The corneal sub-basal nerve plexus was assessed using *in vivo* confocal microscopy, and the ocular surface status was evaluated by tear break-up times.

Results: The mean age of 33 patients with blepharoptosis and 17 normal controls were 38.77 ± 22.81 years and 48.35 ± 17.15 years, respectively. The mean duration of blepharoptosis was 16.42 ± 15.60 years. In 13 patients with unilateral blepharoptosis, there was no significant difference between affected eyes and contralateral eyes (all p s > .05), except for wider corneal nerve fibre width (CNFW) in affected eyes (0.024 ± 0.001 versus 0.023 ± 0.001 mm/mm², $p = .021$). In 20 patients with bilateral blepharoptosis, there was no significant difference between the eyes. No significant difference was detected between 19 cases with congenital blepharoptosis and 14 cases with aponeurogenic blepharoptosis. When compared with normal controls, eyes with both unilateral and bilateral blepharoptosis had significantly wider CNFW. But from the point of aetiology, only eyes with congenital blepharoptosis presented with wider CNFW ($p = .001$), rather than the eyes with aponeurogenic blepharoptosis ($p = .093$). Besides, four young patients with congenital blepharoptosis revealed very sparse sub-basal nerve plexus.

Conclusions: These data suggested that corneal confocal microscopy demonstrated no significant changes in patients with blepharoptosis as compared with normal controls, except for relatively wider CNFW in congenital affected eyes. However, in some children and young adults with congenital blepharoptosis, the density of corneal sub-basal nerve plexus was evidently decreased, which needs to be cautioned when ones with congenital blepharoptosis want to take corneal surgeries or wear contact lens.

KEY MESSAGES

- When compared with normal controls, no significant effect was found in the influence of blepharoptosis on the most of corneal nerve parameters, except for corneal nerve fibre width (CNFW) in the group of congenital blepharoptosis.
- The age of onset of blepharoptosis may influence corneal nerve fibres, so timely surgical treatment of congenital blepharoptosis is not only conducive to the development of normal vision, but also beneficial to the reduction of corneal nerve lesions to some extent.
- We noted that some young blepharoptosis patients revealed sparse corneal nerve, which should be taken precaution when ones with congenital blepharoptosis who want to take corneal surgeries or wear contact lens.

ARTICLE HISTORY

Received 30 July 2021

Revised 5 November 2021

Accepted 24 December 2021

KEYWORDS

Blepharoptosis; cornea; sub-basal nerve plexus; *in vivo* confocal microscopy; automated analysis; ACCMetrics

Introduction

Blepharoptosis is a condition presenting as the downward displacement of the upper eyelid, which can be classified into two primary categories, congenital and

acquired [1]. Congenital blepharoptosis is a drooping or abnormally low of the upper eyelid that is present at birth or within the first year of life. Most cases of congenital blepharoptosis are attributed to

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developmental abnormalities of the levator muscle that is fibrous and/or infiltrated with fatty tissue. Aponeurogenic blepharoptosis, the most encountered type of acquired blepharoptosis and often being diagnosed in the elderly population, is the result of age-related changes in the levator aponeurosis including thinning, stretching, or dehiscence from its tendinous attachments to the superior tarsal plate. Histologic investigation of the encompassing levator muscle in patients with aponeurogenic blepharoptosis proposes a potential age-related myopathic process as a part in the pathogenesis of this condition [2].

The cornea is the outermost tissue of the eye in the front part. It is unique in being the most densely innervated structure and is the most sensitive tissue in the human body [3]. Corneal sensory nerves stem from the ophthalmic branch (V1) of the fifth cranial nerve, providing sensitivity to pain, cold, mechanical, and chemical stimuli. The cornea keeps a rich nerve supply with a high density of nerve fibres situated inside the epithelium, in the sub-basal plexus and anterior stroma [4]. With the advent of *in vivo* confocal microscopy (IVCM), it can be easy and non-invasive to assess morphologic attributes of the corneal nerve bundles such as length, density, tortuosity area, and width, in adults and young children [5–7].

Normally, most part of cornea exposes to environment except for about 2 mm cornea above is covered by upper eyelid in the daytime. In the condition of blepharoptosis, however, about more than half of the cornea above is covered in daily life. Then, whether the corneal nerve changes after a long duration due to less external stimuli? Therefore, the main purpose of our study was, using IVCM, to investigate the long influence of blepharoptosis on the corneal sub-basal nerve plexus (SNP), which was not reported before.

Materials and methods

The protocol was approved by Institutional Review Board of the Affiliated Wuxi Clinical College of Nantong University. Prior to inclusion, written informed consent was obtained from all patients and controls. If a patient's age was less than 18 years old, written informed consent was obtained from her/his legal guardian. Our study adhered to the tenets of the Declaration of Helsinki.

Subjects

In the present study, we only recruited patients with congenital or aponeurogenic blepharoptosis. Subjects

with aponeurogenic ptosis were included if their history revealed a gradually progressive unilateral or bilateral blepharoptosis over 1 year. On examination, the marginal reflex distance (MRD, vertical distance from the corneal light reflex to the central upper eyelid margin with the eyes in primary position) from one or both eyes had to be 1 mm or less. Patients were excluded whose blepharoptosis was possibly (or somewhat) due to other causes than congenital or aponeurogenic. Neostigmine test was administered to exclude myasthenia gravis (MG). For subjects with congenital ptosis, they were included if history revealed a unilateral or bilateral blepharoptosis was present at birth or within the first year of life. In addition, individuals were not eligible if they had active ocular surface disease, diabetes mellitus, treatment for any systemic condition that may affect the ocular surface, any previous ocular surgery or ocular trauma. Contact lens wearers and smokers that may have inverse effect on corneal nerves were also excluded [8,9]. Normal controls who did not suffer from blepharoptosis were matched for sex and age to subjects. All the recruited participants were measured for tear break-up times (BUTs) by a single investigator (Z. W. Z.). BUTs values were determined by commercially available sterile fluorescein paper strips (Jingming New Technological Development Co. Ltd., Tianjin, China). Specifically, a fluorescein strip moistened with normal saline was applied to slightly touch the inferior bulbar conjunctiva. Participants were asked to blink three times naturally and then to look straight ahead without blinking. The time from the last blink to the first dark spot on the tear film was measured under a cobalt-blue filter and broad beam of light from the slit-lamp. The participant was excluded if the BUTs were less than 10 s in both eyes.

In vivo confocal microscopy

Laser scanning *in vivo* confocal microscopy was conducted to determine corneal nerve morphology. The Heidelberg Retinal Tomography III with the Rostock Corneal Module (Heidelberg Engineering GmbH, Heidelberg, Germany) was used and setup according to standard technique [10]. IVCM was performed under topical anaesthesia with one drop of 0.4% Oxybuprocaine Hydrochloride (Santen Ltd, Tokyo, Japan), and the participant was asked to observe a central target and section scans of non-overlapping areas were taken on the central cornea focussing on the SNP layer, typically at a depth of 50–80 μm . All

IVCM examinations were performed by a single experienced examiner (S. L.).

Image analysis

Images were captured from the both eyes. For normal controls, because the data of both eyes have great correlation, in order to reduce the statistical error [11], one eye of each subject was selected at random for image analysis. Five to eight most representative images of corneal SNP that did not overlap by more than 20% were chosen for analysis based on optimal contrast, presence of in-focus nerves and absence of motion artefacts in a masked fashion by the same observer (Z. W. Z.). Images (400 μm in width by 400 μm in height) were analyzed using a fully automated nerve fibre image analysis program [12] (ACCMetrics; Version 2.0, Center for Imaging Sciences, The University of Manchester, UK) to quantify the following parameters as reported previously [13–15]: (1) corneal nerve fibre density (CNFD, the total number of main nerves/ mm^2); (2) corneal nerve branch density (CNBD, the total number of branches stemming from main nerve trunks/ mm^2); (3) corneal nerve fibre length (CNFL, the total length of main nerve fibres and branches per square millimetre, mm/mm^2); (4) corneal nerve fibre total branch density (CTBD, the total number of branches/ mm^2); (5) corneal nerve fibre area (CNFA, the total nerve fibre area per square millimetre, mm^2/mm^2); (6) corneal nerve fibre width (CNFW, the average nerve fibre width per square millimetre, mm/mm^2); (7) corneal nerve fractal dimension (CNFrD, fractional number that describes how the structural complexity of corneal nerve fibres is). A high CNFrD corresponds to an evenly distributed complex and healthier nerve fibre structure, while lower CNFrD values indicate lower geometric nerve complexity potentially indicating abnormality [16].

Statistical analysis

All values of corneal parameters are expressed as the mean \pm standard deviation. Statistical analyses were

performed using SPSS software (version 21.0, SPSS, Chicago, IL). A one-sample Kolmogorov–Smirnov test was used to assess the normal distribution of continuous variables before a test of significance. As a result, all the continuous variables were normally distributed. The corneal parameters between left and right eyes (or between affected eyes and contralateral eyes) using paired Student's *t*-test. The difference of continuous variables between two independent groups were assessed by independent sample *t*-test. Data among different groups (congenital blepharoptosis, aponeurogenic blepharoptosis and normal controls) were analyzed using one-way analysis of variance (ANOVA) and the Bonferroni post-hoc test. Chi-square test was applied to analyze the categorical variables. Correlations between variables were analyzed using Pearson partial analysis. $p < .05$ was considered statistically significant. All tests were two-tailed.

Results

Thirty-three patients with blepharoptosis (20 bilateral and 13 unilateral) and 17 normal controls who referred to the Department of Ophthalmology, Affiliated Wuxi Clinical College of Nantong University were enrolled. The demographic data of all the participants are presented in Table 1. Patients with bilateral blepharoptosis varied in age from 8 to 76 years (mean age, 34.96 ± 24.84 years) and patients with unilateral blepharoptosis varied in age from 18 to 69 years (mean age, 42.45 ± 18.95 years), with normal controls varying in age from 15 to 70 years (mean age, 48.35 ± 17.15 years). The duration of bilateral and unilateral blepharoptosis was 14.7 ± 14.91 years (range, 2–70 years) and 19.08 ± 16.87 years (range, 1–66 years), respectively. No significant differences were found for age and sex between blepharoptosis patients and normal controls (always $p > .05$).

Representative IVCM images analyzed with ACCMetrics are shown in Figure 1. The values of each IVCM parameter obtained with the software ACCMetrics in the blepharoptosis patients and normal controls were listed in Tables 2–4. For patients with

Table 1. Demographic results and clinical profiles of blepharoptosis patients and normal controls.

	Bilateral	Unilateral	Control	<i>p</i> Value	P1	P2	P3
<i>N</i> (male/female)	20 (8/12)	13 (5/8)	17 (6/11)	0.957 ^a	NA	NA	NA
Age (years, range)	34.96 ± 24.84 (8–76)	42.45 ± 18.95 (18–69)	48.35 ± 17.15 (15–70)	0.178 ^b	0.973	1.000	0.234
Time since ptosis onset (years, range)	14.7 ± 14.91 (2–70)	19.08 ± 16.87 (1–66)	N/A	0.440 ^c	NA	NA	NA

NA: not applicable. ANOVA with Bonferroni post-hoc analysis between individual groups: P1: bilateral versus unilateral; P2: bilateral versus controls; P3: unilateral versus controls.

^aChi-square test.

^bOne-way ANOVA.

^cIndependent sample *t* test.

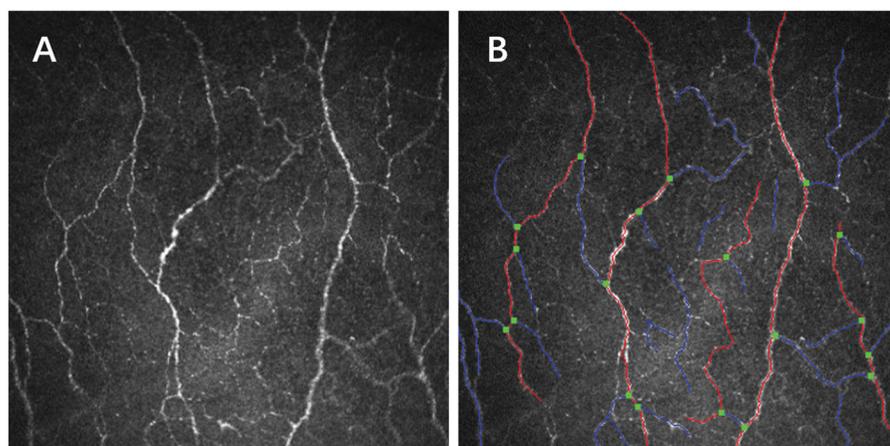


Figure 1. (A) Representative *in vivo* confocal microscopy image ($400\ \mu\text{m} \times 400\ \mu\text{m}$) of corneal sub-basal nerve plexus obtained from the central cornea of a patient with blepharoptosis. (B) Fully automated image analysis using ACCMetrics software with main nerve fibres being indicated in red, nerve branches in blue and branch points in green.

Table 2. Confocal microscopy data of bilateral blepharoptosis patients and normal controls.

	OD (N = 20)	OS (N = 20)	Both eyes (N = 40)	Control (N = 17)	P1	P2	P3
Corneal nerve fibre density (n/mm ²)	17.19 ± 8.05	15.03 ± 8.01	16.11 ± 8.00	18.98 ± 6.34	0.142	0.463	0.110
Corneal nerve branch density (n/mm ²)	22.42 ± 16.60	18.45 ± 14.89	20.44 ± 15.69	23.85 ± 13.18	0.105	0.777	0.254
Corneal nerve fibre length (mm/mm ²)	12.21 ± 4.32	11.77 ± 3.70	11.99 ± 3.98	13.05 ± 3.04	0.553	0.508	0.265
Corneal nerve fibre total branch density (n/mm ²)	36.31 ± 22.03	32.48 ± 21.00	34.39 ± 21.33	40.27 ± 20.12	0.327	0.574	0.260
Corneal nerve fibre area (mm ² /mm ²)	0.0057 ± 0.002	0.0091 ± 0.016	0.007 ± 0.011	0.007 ± 0.002	0.351	0.158	0.514
Corneal nerve fibre width (mm/mm ²)	0.023 ± 0.001	0.023 ± 0.002	0.023 ± 0.001	0.022 ± 0.001	0.999	0.006	0.020
Corneal nerve fractal dimension	1.45 ± 0.05	1.45 ± 0.04	1.45 ± 0.04	1.46 ± 0.03	0.953	0.342	0.285

P1: paired sample *t* test between OD and OS; P2: independent sample *t* test between OD and controls; P3: independent sample *t* test between OS and controls.

bilateral blepharoptosis, there was no significant difference between both eyes in all IVCN parameters (Table 2). However, CNFW was significantly higher both in the right eyes ($0.023 \pm 0.001\ \text{mm}/\text{mm}^2$, $p = .006$) and left eyes ($0.023 \pm 0.002\ \text{mm}/\text{mm}^2$, $p = .020$) than in the controls ($0.022 \pm 0.001\ \text{mm}/\text{mm}^2$) (Table 2). For patients with unilateral blepharoptosis, there was no significant difference between both eyes in most IVCN parameters, except that CNFW was significantly higher in the affected eyes ($0.024 \pm 0.001\ \text{mm}/\text{mm}^2$) than in the contralateral eyes ($0.023 \pm 0.001\ \text{mm}/\text{mm}^2$, $p = .021$) and normal controls ($0.022 \pm 0.001\ \text{mm}/\text{mm}^2$, $p = .001$) (Table 3).

However, from the point of aetiology, when compared with normal controls ($0.022 \pm 0.001\ \text{mm}/\text{mm}^2$), only eyes with congenital blepharoptosis presented with higher CNFW ($0.024 \pm 0.002\ \text{mm}/\text{mm}^2$, $p = .006$), rather than the eyes with aponeurogenic blepharoptosis ($0.023 \pm 0.001\ \text{mm}/\text{mm}^2$, $p = .093$) (Table 4). Except for CNFW, we did not detect significant difference between patients and normal controls (always $p > .05$).

Besides, no significant correlation was found between the duration of blepharoptosis and corneal parameters (always $p > .05$, Pearson partial analysis, adjusting for age). Age also did not significantly correlate with corneal parameters (always $p > .05$, Pearson

partial analysis, adjusting for the duration of blepharoptosis). In addition, four young patients with congenital blepharoptosis revealed very sparse sub-basal nerve plexus.

Discussion

To the best of our knowledge, there are no published data that reveal the effects of blepharoptosis on the cornea using IVCN in previous studies. Despite the fact that being to a great extent undetectable on regular assessment procedures, the approach of IVCN has empowered *en face* assessment of corneal nerves in health and disease [4,7]. Furthermore, some customized software programs have allowed quantification of various aspects of nerve morphology including fibre length, density, width, tortuosity, branching, beading and reflectivity [5,17]. ACCMetrics, a fully automatic software program that was employed in the present study, is now widely accepted to quantify a comprehensive morphometric analysis of all the characteristics of the corneal sub-basal nerve plexus [18–20].

Unexpectedly, we found no significant difference of most corneal nerve parameters between eyes with bilateral or unilateral blepharoptosis and normal controls, except for eyes with blepharoptosis having

Table 3. Confocal microscopy data of unilateral blepharoptosis patients and normal controls.

	Blepharoptosis eyes (N = 13)	Contralateral eyes (N = 13)	Both eyes (N = 26)	Control (N = 17)	P1	P2	P3
Corneal nerve fibre density (n/mm ²)	15.73 ± 8.74	15.18 ± 6.16	15.45 ± 7.41	18.98 ± 6.34	0.813	0.247	0.111
Corneal nerve branch density (n/mm ²)	20.41 ± 15.59	19.48 ± 12.00	19.94 ± 13.64	23.85 ± 13.18	0.714	0.518	0.359
Corneal nerve fibre length (mm/mm ²)	11.22 ± 3.75	11.00 ± 2.84	11.11 ± 3.26	13.05 ± 3.04	0.743	0.153	0.071
Corneal nerve fibre total branch density (n/mm ²)	38.27 ± 24.43	33.15 ± 13.86	35.71 ± 19.63	40.27 ± 20.12	0.237	0.807	0.285
Corneal nerve fibre area (mm ² /mm ²)	0.005 ± 0.002	0.005 ± 0.001	0.006 ± 0.002	0.007 ± 0.002	0.093	0.322	0.054
Corneal nerve fibre width (mm/mm ²)	0.024 ± 0.001	0.023 ± 0.001	0.023 ± 0.001	0.022 ± 0.001	0.021	0.001	0.131
corneal nerve fractal dimension	1.45 ± 0.05	1.44 ± 0.04	1.44 ± 0.05	1.46 ± 0.03	0.574	0.212	0.117

P1: paired sample *t* test between blepharoptosis eyes and contralateral eyes; P2: independent sample *t* test between blepharoptosis eyes and controls; P3: independent sample *t* test between contralateral eyes and controls.

Table 4. Confocal microscopy data of congenital, aponeurogenic blepharoptosis patients, and normal controls.

	Congenital ^a (N = 19)	Aponeurogenic ^a (N = 14)	Control (N = 17)	<i>p</i> ^b	P1	P2	P3
Age (years)	22.23 ± 7.80	64.90 ± 8.73	51.71 ± 17.72	<.001	<0.001	<0.001	0.014
Time since ptosis onset (years, range)	15.68 ± 5.86	17.43 ± 23.45	N/A	.789 ^c	NA	NA	NA
Corneal nerve fibre density (n/mm ²)	17.36 ± 8.81	12.51 ± 6.53	18.98 ± 6.34	.102	0.184	1.000	0.169
Corneal nerve branch density (n/mm ²)	20.56 ± 15.81	17.40 ± 14.09	23.85 ± 13.18	.672	1.000	1.000	1.000
Corneal nerve fibre length (mm/mm ²)	12.58 ± 3.93	10.17 ± 2.85	13.05 ± 3.04	.08	0.147	1.000	0.133
Corneal nerve fibre total branch density (n/mm ²)	34.46 ± 21.77	35.18 ± 23.64	40.27 ± 20.12	.771	1.000	1.000	1.000
Corneal nerve fibre area (mm ² /mm ²)	0.009 ± 0.016	0.006 ± 0.002	0.007 ± 0.002	.309	1.000	0.932	0.407
Corneal nerve fibre width (mm/mm ²)	0.024 ± 0.002	0.023 ± 0.001	0.022 ± 0.001	.001	0.524	0.001	0.093
Corneal nerve fractal dimension	1.46 ± 0.04	1.44 ± 0.04	1.46 ± 0.03	.114	0.265	1.000	0.154

ANOVA with Bonferroni post-hoc analysis between individual groups: P1: congenital versus aponeurogenic; P2: congenital versus controls; P3: aponeurogenic versus controls.

^aIn order to reduce statistical error, only the data of right eyes of bilateral congenital or aponeurogenic blepharoptosis were chose to statistically analyze.

^bANOVA between congenital, aponeurogenic blepharoptosis and controls.

^cIndependent sample *t* test.

significantly higher value of CNFW (Tables 2 and 3). Interestingly, in cases with unilateral blepharoptosis, CNFW value was higher in affected eyes than contralateral eyes (Table 3), that was not the case for eyes with bilateral blepharoptosis (Table 2). When compared with normal controls, eyes with both unilateral and bilateral blepharoptosis had significantly higher CNFW value (Tables 2 and 3). But from the point of aetiology, only eyes with congenital blepharoptosis presented with higher CNFW value ($p = .001$), rather than the eyes with aponeurogenic blepharoptosis ($p = .093$) (Table 4). This indicates that the age of onset of blepharoptosis may have an effect on corneal nerve fibres. Therefore, timely surgical treatment of congenital blepharoptosis is not only conducive to the development of normal vision but also beneficial to the reduction of corneal nerve lesions to a certain extent.

Previously, an increased CNFW value was also reported in patients with dry eye diseases analyzed by ACCmetrics [15]. This morphological change may be caused by the missing of smaller corneal nerve fibres but with the conservation of thicker trunks. Besides, this microstructural alteration was also reported in young patients with type 1 diabetes mellitus [21] or cases with sarcoidosis-associated neuropathy [22]. In this sense, blepharoptosis might undermine corneal

smaller nerve fibres in a long run. However, no significant correlation was detected between all the corneal parameters and duration of blepharoptosis, including CNFW (all $ps > .05$). This may require further research on a larger sample size.

Another surprising finding was that the corneal nerves of both eyes were very sparse in 4 young patients (younger than 25 years old, 2 unilateral and 2 bilateral congenital blepharoptosis) when compared with normal young subjects (Figure 2). However, we found no case with very sparse corneal nerves in eyes of the normal controls. This reminds us that young patients with a previous history of blepharoptosis need to be particularly cautioned if they need corneal surgeries or wear contact lens. For the two cases with unilateral blepharoptosis, it was curious that sparse corneal nerves affected both eyes. Thinking about the apprehensive association between the two eyes, one eye's condition might decide contralateral corneal nerves changes also. Developing proof recommended the presence of the bilateral sympathetic effect of affected and unaffected eyes in some ocular diseases or ocular surgery [14,23]. More recently, Giannaccare et al. [14] reported that patients undergoing unilateral microincisional cataract surgery showed bilateral alterations of corneal sub-basal nerve plexus even 30 days postoperatively. It is still not explicit whether these

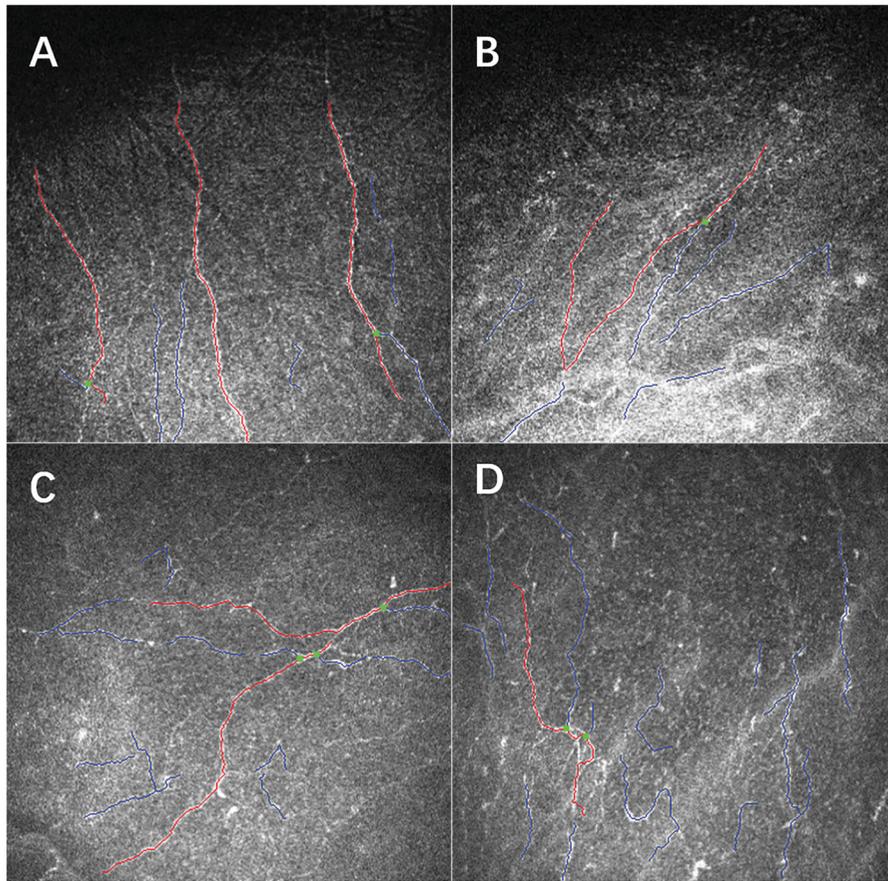


Figure 2. Representative *in vivo* confocal microscopy images young patients with congenital blepharoptosis revealed very sparse sub-basal nerve plexus. A young patient of 20 years old with unilateral blepharoptosis in his right eye revealed sparse sub-basal nerve plexus (A), as did in his left eye (B). A teenage boy with bilateral blepharoptosis revealed sparse sub-basal nerve plexus in his both eyes (C, D).

findings have a biological significance or are only an epiphenomenon. For all that, these effects may indicate the presence of signalling mechanisms that couple the two sides of the body at a central or peripheral level [24].

In a previous study with 343 normal controls, Tavakoli et al. [6] employed a semi-automated software “CCmetrics” and reported a significant linear age-dependent decrease in CNFD, CNFL and CNFT, but without change with age in CNBD. However, we did not find any correlation between corneal parameters and age in both eyes with blepharoptosis and normal controls (all $ps > .05$). In a study recruited 20 healthy Chinese subjects with mean age of 44.10 ± 7.28 years (comparable to age of our normal controls, 36.22 ± 19.38 years) and analyzed images with ACCMetrics as well [20], CNFD (18.98 ± 6.34 versus 28.4 ± 6.7), CNBD (23.85 ± 13.18 versus 41.9 ± 16.0), CNFL (13.05 ± 3.04 versus 17.6 ± 3.6) and CTBD (40.27 ± 20.12 versus 56.5 ± 19.8) were relatively lower in our study than in theirs. However, CNFA

(0.007 ± 0.002 versus 0.007 ± 0.002), CNFW (0.022 ± 0.001 versus 0.022 ± 0.001) and CNFrD (1.5 ± 0.03 versus 1.46 ± 0.03) were comparable. These findings may suggest a relatively big variation of some corneal nerve parameters in individuals.

Corneal nerve fractal dimension (CNFrD) is a newly developed IVCN parameter obtained with employment of the latest version of ACCMetrics program [25,26]. CNFrD indicates the structural complexity of corneal nerve fibres, which could be useful as an alternative means to identify patients with neuropathies of various causes. Recently, Chen et al. [16] reported that CNFrD has sufficient discriminatory potential as good as conventional IVCN parameters to differentiate patients with corneal diabetic neuropathy from normal controls. In the present study, CNFrD was measured for the first time in patients with blepharoptosis. However, no significant difference in CNFrD value was found between cases with blepharoptosis and control subjects, as reported in patients with dry eye diseases [15]. Further studies with large sample size

are warranted to clarify the role of CNFrD in different causes.

There are a few notable limitations to this preliminary study. First, the sample size was relatively small. However, we established strict inclusion criteria, which could reduce the influence of other confounding factors on the results to some extent. Second, corneal sensitivity and Schirmer test did not perform because of objective reasons, but we excluded subjects whose BUTs were less than 10 s. One previous study using Schirmer-I test reported that patients with acquired aponeurogenic blepharoptosis more often had a decreased aqueous tear production, but the frequency of BUTs < 10s was comparable between the two groups [27]. Therefore, if we excluded patients with BUTs < 10s, we can minimize the influence of dry eye on corneal nerve. Third, most of patients are loss of follow-up more than one year after surgery. It may be interesting to follow up the changes of corneal nerve for a long time after surgical correction of blepharoptosis.

Conclusions

In summary, our study represents the first investigation of the influence of blepharoptosis on the corneal nerve and no significant effect was found, except for CNFW. The higher value of CNFW might imply the loss of smaller nerve fibres but with the preservation of thicker bundles. We found that the age of onset of blepharoptosis may influence corneal nerve fibres, so timely surgical treatment of congenital blepharoptosis may be beneficial to the reduction of corneal nerve lesions to some extent. Besides, we noted that some young blepharoptosis patients revealed sparse corneal nerve, which should be taken precaution when ones with congenital blepharoptosis who want to take corneal surgeries or wear contact lens.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This study was supported by the fund of Top Talent Support Program for young and middle-aged people of Wuxi Health Committee [Grant no. HB2020030] and the Development Fund of Wuxi Science and Technology [Grant no. WX18IIAN019].

Data availability statement

The data used to support the findings of this study are available from the corresponding author upon request.

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